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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,091	11/25/2003	Jose Remacle	4044.001	7897

7590 12/19/2006

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/06 has been entered.

Status of Claims

Claims 1-20 are pending and under examination.

Withdrawn Rejections

In view of the amendments to the claims and applicants' arguments, the 35 USC 102 rejection over Decker and Devereaus is withdrawn. Likewise, the 103 rejection over Decker et al in view of Brennan et al or applicants' disclosure of prior art is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

> use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed "simultaneously contacting a C5 to C7 polyol with a protein contained in a spotting solution or being present on an array" is not supported in the as filed specification.

Applicants pointed out support at page 12, paragraphs 57-58 and page 15, paragraphs 71-72.

A review of these cited sections do not recite for a simultaneous contacting of a C5 to C7 polyol with a protein solution. (See further the 112, 2nd paragraph rejection below).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1, step a) recitation of "contacting a C5 to C7 polyol simultaneously with a protein contained in a spotting solution or being present on an array" is confusing. Is the polyol added or mixed with the protein to form the spotting solution and the solution then spotted to the array? The alternative phrase "or being present on an array" is confusing as to whether the protein is already present or simultaneously added with the spotting solution containing the polyol.

Step c) is unclear as to the step of allowing covalent fixation of the proteins on the surface of the support. Is it only the proteins that are covalently fixed on the surface of the support? The inconsistent used of terminologies e.g., "analyte-specific regions", "a selected capture protein" in the preamble and "protein" in the body provides for confusion. It is not clear whether these different terminologies apply to one and the same protein. The term "analyte-***specific*** regions", in the context of the claim, is indefinite as to the measure or basis by which specificity to the analyte is determined in the absence of any kind or structure of the analyte or capture protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5 and 8-12, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Stillman et al (20030175827).

Stillman discloses at paragraph [0010] a method for producing a thin film dried protein composition comprising making a protein containing solution that is to be dried on a surface, preferably a biologically active protein. The term "biologically active" includes any protein that can participate in a specific binding reaction, (such as antibodies, antibody fragments, antigens, antigen fragments), as well as peptides or enzymes.) The solution is made with a buffer that maintains the surface pH between about 5.0 and 9.0 during solution drying and with a saccharide in an amount sufficient to stabilize the

protein during solution drying. The solution is then applied to a support having the surface for depositing. Thin film of protein containing solution is allowed to dry on the support surface under normal pressures. At paragraph [0011] the method enables one to make stable thin film dried protein compositions. Such films can be incorporated into protein analytical devices. of particular interest are proteomic microarrays.

Response to Arguments

Applicants recognize that Stillman et al discusses a method for the preparation of a stable thin, film dried protein composition on a surface of e.g. a solid support. A thin film of a protein containing solution is applied to the surface of a solid support together with a saccharide, such as xylitol or mannitol, for stabilizing the protein during drying. But argue that Stillman does not teach or disclose polyols linked to other molecules nor the covalent binding of the peptides to the support.

In response, applicants' arguments that the polyols are linked to other molecules are not commensurate in scope with e.g., claim 1. Nonetheless, attention is drawn to paragraph [0018}. Furthermore, it is considered that the protein of Stillman would be inherently covalent bonded to the surface of the support since stability and reaction to the target protein

did not denature the proteins on the support. See further paragraphs [0023] and [0024].

Claim Rejections - 35 USC § 103

Claims 1-15 and 18-20, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Decker(GB 2,016,687A) or Devereaus (WO 93/07466) or Stillman in view of either Guo(Faming Zhuanli Shenqing Gongkai) or Sandford (US 2003/0134294) and Schultz et al(20040198637).

Decker discloses at pages 2 up to 5 an immunoassay method for the detection and determination of antigens and antibodies. The method comprises an indirect application of an antibody or antigen to a solid support (a selected capture protein, as claimed). It generally involves the procedure in which the solid support is precoated with antigen or antibody to potentiate the adherence of the antibody or antigen. The reagents consist of a solid support that has been coated either directly or indirectly with an antigen or antibody and stabilized with a sugar coating to impart a storage capability. The percent of sugar e.g., xylitol, mannitol and sorbitol is given in Table II.

Devereaus discloses at e.g., page 14, line 16 up to page 15, line 25 a method (i.e., the use of .1-50% of polyol, specifically arabitol and xylitol). See specifically the EXAMPLES, which provide a detail description of the claimed method using specific components in the array.

Stillman is discussed above.

Each of Decker, Stillman and Devereaus does not disclose the use of antiseptic as sodium azide and that the protein is covalently linked to the solid support. However, Guo discloses in the abstract a method in which a protein chip with array of 10-10,000 cm-1 and array size of 5-500 consists of the activated carrier and spotting solution. The spotting solution is composed of probe (such as antigen, antibody, drug receptor, agglutinin, cell, or tissue), fucose, antiseptic (such as Na azide) and C2-10 aliphatic polyol. The protein chip is manufactured by spotting the mixture of probe and spotting solution on the activated carrier sheet, and then blocking with bovine serum. The protein chip may be used to detect, recognize, and identify the antigen, antibody, medicine or its receptors, polysaccharide, agglutinin, tissue, or cell.

Sandford discloses at paragraph [0197] that preservatives like azide are effective to retard or prevent microbial proliferation. Sandford discloses at paragraph [0199]

Lyoprotectants are effective to reduce or prevent chemical or physical instability of a protein upon lyophilization and storage. Examples of a polyol such as trihydric or higher sugar alcohol (e.g., glycerin, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol). Sandford also discloses the use of borate buffer.

Schultz et al discloses:

[0101] In one embodiment, the polypeptides are provided in a reaction mixture that is suitable for the necessary reaction between the reactive group on the unnatural amino acid side chain and the reactive group attached to the solid support. For a nucleophilic reaction between an aldehyde or ketone and a nucleophilic moiety such as a hydrazine derivative, a slightly acidic pH is generally preferred; sufficiently acidic so that an appreciable fraction of the carbonyl groups are protonated, but not so acidic that the free nitrogen compound is too low in concentration. In some embodiments, the polypeptides remain hydrated throughout the preparation, storage, and assaying of the array to prevent denaturation of the polypeptide. Accordingly, humectants or polymers such as glycerol, polyethylene glycol, glycerin, **maltitol**, polydextrose, sorbitol, cetyl alcohol, fatty alcohols, propylene glycol, and the like, can be used to prevent evaporation of the nanodrops. One can also provide the polypeptides in organic solvents (e.g., DMSO, DMF) or in partially aqueous solutions (e.g., 10% DMSO in water).

[0048] Systems for immobilizing polypeptides on a solid support, as well as the resulting solid supports containing the polypeptides, e.g., protein arrays, are provided. The systems allow one to covalently or non-covalently attach the polypeptides to the solid support in such a manner as to preserve the function of the polypeptides or to regain their functionality once attached. The covalent or non-covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other

> polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.). The protein arrays of the invention are versatile and can be adapted to a variety of protein analysis formats. The arrays find use in a wide variety of applications, including numerous types of screening protocols and any protein analysis where high throughput parallel analysis is desirable.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use azide in the method of either Decker or Stillman or Devereaus as taught by either Sandford or Guo. The advantages taught by Sandford or Guo would provide the motivation to one having ordinary skill in the art as to the known use of azide as a preservative. Furthermore, as taught by Schultz the protein can be covalently or non-covalently link to the array in a manner that preserves its function.

Response to Arguments

Applicants acknowledge that Decker et al. relates to the stabilization of protein arrays with sugars. But states that Decker discloses a protein is applied directly or by means of a spacer to a solid support and afterwards stabilized by coating with sugar containing solution, such as 10% mannitol on phosphate buffered saline. Furthermore, Decker specifies a different order of method steps, i.e. a stabilization step subsequent a coating step with protein (Decker, p. 2, lines 12

to 15). Decker also does not teach or disclose a protein deposition on discrete regions of the solid support, nor, the use of polyols linked to other molecules is not disclosed.

In response, the claims ("being present on an array, claim 1) also recite in the alternative applying the protein directly on the support, after which the polyol is spotted on the surface. It is unclear as to how Decker method steps are in different order. As clearly discussed above by applicants the protein of Decker is applied directly to a solid support and then sugar is added on the surface. As stated above, the arguments as to the polyols being linked to other molecules is not a limitation present in the claims. Nonetheless, Schultz discloses the use of a polyol linked to other molecule e.g., maltitol.

Since applicants present the same arguments to rebut Devereaus, hence the response under Decker above is applied to Devereaus.

Applicants argue that Guo does not teach at the use of C5-C7 polyols, which preserve the activity of proteins in a microarray. Sandford does not teach or disclose simultaneous contacting of a protein and a polyol neither linked to another molecule with the support nor specifies drying of the spotting

solution. Additionally Sanford does not mention a protein deposition on discrete regions of the support.

In response, Guo discloses C2-10 aliphatic polyol, which includes the claimed range of C5-C7 polyol. It is believed that the polyol is used for the same purpose of preserving protein in microarray since the same process and components are used by Guo. It is well known in the art that the polyol is used as preservative for protein on a microarray. Note that the claims do not also recite that the polyol are use to preserve the protein microarray.

Sanford is employed not for the purpose as argued since the primary references e.g., Stillman discloses the method of mixing of the spotting solution for the microarray. Rather, Sanford is used for its disclosure of using a borate buffer and the motivation for one having ordinary skill in the art to include a borate in the solution of e.g., Stillman.

Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Decker or Devereaus or Stillman in view of either Guo(Faming Zhuanli Shenqing Gongkai) or Sandford (US 2003/0134294) and Schultz as applied to claims 1-15 and 18-20 above, and further in view of in view of Moreadith (USP 6632934).

Each of Decker, Stillman and Devereaus does not disclose that the microarray containing protein can be stored for more than six months. Moreadith discloses at col. 24, lines 23-35 that in general, due to the relative stability of peptides, they may be readily stored in aqueous solutions for fairly long periods of time if desired, e.g., up to six months or more, in virtually any aqueous solution without appreciable degradation or loss of antigenic activity. However, where extended aqueous storage is contemplated it will generally be desirable to include agents including buffers such as Tris or phosphate buffers to maintain a pH of about 7.0 to about 7.5. Moreover, it may be desirable to include agents which will inhibit microbial growth, such as sodium azide. For extended storage in an aqueous state it will be desirable to store the solutions at about 4.degree. C., or more preferably, frozen. Of course, where the peptides are stored in a lyophilized or powdered state, they may be stored virtually indefinitely, e.g., in metered aliquots that may be rehydrated with a predetermined amount of water (preferably distilled) or buffer prior to use. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to store the composition of any one of Decker or Stillman and Devereaus for more than six months as taught by Moreadith. Each of Decker, Stilmann or

Devereaus teaches polyol as a stabilizer as similarly claimed. [Note that Decker teaches said storage for a long period of time employing the polyol as stabilizer except did not positively teach the length of time i.e., months it can be stored.]

Response to Arguments

Applicants argue that Moreadith neither relates to protein arrays nor specifies the usage of polyols linked to other molecules for immobilizing arrays. Stillman relates to short term stabilization of protein arrays to avoid e.g. denaturation during drying. None of these references teach contacting a C5 to C7 polyol simultaneously with a protein contained in a spotting solution or being present on an array, wherein said polyol is between 0.5 and 10% of the spotting solution, depositing the spotting solution on one of the discrete regions of the surface of a solid support, allowing covalent fixation of the proteins on the surface of the support, allowing the spotted solution to dry on the support wherein the protein retain 70% of their activity when stored in periods of 6 to 12 months.

In response, the response to Stillman above is incorporated herein since applicants merely repeat their arguments in Stillman as herein. Moreadith is not used for the purpose as

argued i.e., protein arrays. Moreadith is used for its teachings that protein can be stored for more than 6 months and the use of antimicrobial agent, azide. One cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968). The test for obviousness under 35 USC 103 is not the express suggestion of the claimed invention in any or all of the references but what the references taken collectively would suggest; and inferences which one skilled it in the art would reasonably be expected to drawn from the disclosure in the references. In re Preda, 159 USPQ 342 and In re Conrad, 169 UASPQ 170. Thus, the combined teachings of the prior art would lead one having ordinary skill in the art at the time the invention was made. Moreadith discloses that protein can be stored for more than six months using an antimicrobial agent. Stillman, for example, discloses a method by which a protein is contained in a microarray. It would be within the ordinary skill in the art to use an antimicrobial agent, as sodium azide for the obvious reason of stabilizing protein, whether the protein is present or not on a microarray. The argued concentration of polyol in a solution is a result effective variable well within the ordinary skill determination. This is recognized by applicants at page 8, paragraph [00041] of the disclosure. It

states that in general, the concentration of the polyol contained in the spotting solution may preferably be in the range of between about 0.5 to 10 %, preferably 1 % and 5 %, to show the desired effect.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
December 8, 2006